Tamsulosin and Spontaneous Passage of Ureteral Stones in Children: A Multi-Institutional Cohort Study

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Abbreviations and Acronyms

CT = computerized tomography
ED = emergency department
MET = medical expulsive therapy
UPJ = ureteropelvic junction
UVJ = ureterovesical junction

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Purpose: Tamsulosin is associated with increased passage of ureteral stones in adults but its effectiveness in children is uncertain. We determined the association between tamsulosin and the spontaneous passage of ureteral stones in children.

Materials and Methods: We performed a multi-institutional retrospective cohort study of patients 18 years or younger who presented between 2007 and 2012 with ureteral stones up to 10 mm and who were treated with tamsulosin or oral analgesics alone. The outcome was spontaneous stone passage, defined as radiographic clearance and/or patient report of passage. Subjects prescribed tamsulosin were matched with subjects prescribed analgesics alone, using nearest neighbor propensity score matching to adjust for treatment selection. Conditional logistic regression models were used to estimate the association between tamsulosin and spontaneous passage of ureteral stones, adjusting for stone size and location.

Results: Of 449 children with ureteral stones 334 were eligible for inclusion, and complete data were available for 274 patients from 4 institutions (99 receiving tamsulosin, 175 receiving analgesics alone). Following case matching, there were no differences in age, gender, weight, height, stone size or stone location between the 99 subjects prescribed tamsulosin and the 99 propensity score matched subjects prescribed analgesics alone. In the tamsulosin cohort 55% of ureteral stones passed, compared to 44% in the analgesics alone cohort ($p = 0.03$). In multivariate analysis adjusting for stone size and location tamsulosin was associated with spontaneous passage of ureteral stones (OR 3.31, 95% CI 1.49–7.34).

Conclusions: The odds of spontaneous passage of ureteral stones were greater in children prescribed tamsulosin vs analgesics alone.

Key Words: comparative effectiveness research, nephrolithiasis, tamsulosin

Nephrolithiasis has become increasingly common in children. Among adolescents the incidence of nephrolithiasis has increased approximately 6% to 10% yearly during the last 20 years.[1,2] The emergence of nephrolithiasis as a pediatric disease has resulted in the need to determine the optimal treatment strategies for children with kidney stones.

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In adults alpha-blockers increase the spontaneous passage rates of ureteral stones, decrease time to stone passage and reduce analgesic requirements.[3–5] Furthermore, the use of alpha-blockers as MET for distal ureteral stones in adults is cost effective relative to analgesics alone.[6] However, few studies have assessed the efficacy of MET for ureteral stones in children. A study in 2009 did not reveal any improvement in the passage of distal ureteral stones in children treated with doxazosin.[7] However, the study was likely under powered to detect a clinically important and statistically significant effect. Mokhless et al subsequently observed that tamsulosin increased stone passage in children.[8] However, that study was limited by the inclusion of children who had retained ureteral stones following lithotripsy or percutaneous nephrolithotomy in the tamsulosin group but not in the placebo group. It is possible that the spontaneous passage rates of residual fragments postoperatively are different than in newly diagnosed stones. Additionally these studies excluded children with stones in the proximal or mid ureter, which limits their generalizability. Consequently the effectiveness of tamsulosin in increasing the spontaneous passage of ureteral stones in children who present with new symptomatic ureteral stones is uncertain.

We report the results of a multi-institutional retrospective cohort study designed to determine the association between tamsulosin and the spontaneous passage of ureteral stones in pediatric patients. We hypothesized that tamsulosin increases the spontaneous passage of ureteral stones in children.

METHODS

Patient Cohort Description and Study Design

This was a multi-institutional retrospective cohort study. Potentially eligible subjects were males and females 2 to 18 years old who presented between January 1, 2007 and December 31, 2012 to the ED, outpatient urology clinic or inpatient urology hospital consult service with a ureteral stone, and who were prescribed either tamusolin and oral analgesics or oral analgesics alone. We chose 2007 as the study start date because MET was gaining acceptance for the management of ureteral stones in children at our institutions at that time. Potentially eligible patients were identified by searching outpatient and hospital billing databases for nephrolithiasis ICD-9 codes (592, 592.1, 592.9) at each study site.

We excluded patients who underwent surgical intervention within 24 hours of presentation, those with a history of ureteral or kidney surgery, those with stones greater than 10 mm and those with a clinical contraindication to a trial of stone passage. Patients were excluded if they had a urinary tract infection (temperature greater than 38C and/or positive urine culture), solitary kidney, immunocompromised status (oncologic condition, daily steroid use, bone marrow or solid organ transplant, absolute neutrophil count less than 500 or active use of immunomodulator drug), renal insufficiency (estimated glomerular filtration rate less than 60 ml per minute as estimated by nuclear glomerular filtration rate, cystatin C or bedside Schwartz formula) and/or contraindication to tamsulosin (eg sulfa allergy). Data were abstracted using manual chart review, which was performed separately at each study site. Subjects with missing data were excluded from the analyses.

Outcome Definition

The primary outcome was spontaneous passage of a ureteral stone. Passage was defined as radiographic clearance and/or patient report of passage. All those who did not pass stones within 6 weeks underwent ureteral stent placement and/or ureteroscopy. Additional indications for surgical management included pain refractory to oral analgesics and/or repeat visits to the ED.

Exposure Variable and Covariates, and Sample Size Calculation

The cohort defining variable was prescription of 0.4 mg tamsulosin daily as documented by consultation or clinic notes, or ED discharge notes. The capsule was broken and the drug was sprinkled into a drink, yogurt or pudding for those children who could not swallow the capsule. Covariates included age, height, weight, symptoms at presentation (pain, vomiting, hematuria, voiding symptoms), stone size (mm) and stone location. Stone location was a categorical variable defined as UPJ, mid ureteral or UVJ. Ultrasound, CT and/or abdominal x-ray were used to confirm stone size and location. At 80% power and 2-sided $\alpha = 0.05$ a total of 160 subjects (80 per study group) would be needed to detect a 15% difference in the frequency of spontaneous stone passage between subjects who did and did not receive tamsulosin.

Propensity Score Matching

A panel of 4 pediatric urologists (GET, NGC, CFG, JAF) identified patient and stone characteristics that could influence the decision to prescribe tamsulosin for a child with a ureteral stone. Characteristics identified were age, gender, height and weight, and stone size and location. These independent variables were included in a logistic regression model with tamsulosin prescription as the dependent variable. Age, height and weight were analyzed as continuous variables. Stone size was grouped into 4 strata, ie less than 3 mm, 3 to 5 mm, greater than 5 to 7 mm and greater than 7 to 10 mm. Size was analyzed as a categorical variable to facilitate matching and allow further exploration of an association between size and passage in regression analyses. Stone location was analyzed as a categorical variable, as described previously. The resultant beta coefficients represented the propensity score, ie probability of tamsulosin prescription.

Children prescribed tamsulosin were matched to children prescribed analgesics on the basis of the propensity score using nearest neighbor matching with replacement. After sorting all subjects on their propensity score each subject who received tamsulosin was